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Intracranial multimodal monitoring in neurocritical care (Neurocore-iMMM): an open, decentralized consensus

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Abstract

Background Intracranial multimodal monitoring (iMMM) is increasingly used in neurocritical care, but a lack of standardization hinders its evidence-based development. Here, we devised core outcome sets (COS) and reporting guidelines to harmonize iMMM practices and research.

Methods An open, decentralized, three-round Delphi consensus study involved experts between December 2023 and June 2024. Items—spanning three domains: (i) patient characteristics, (ii) practices, and (iii) outcomes—with ≥ 75% agreement were classified as strong agreement, while those with 50–75% were reconsidered in subsequent rounds, requiring ≥ 66% for moderate agreement.

Results An international, multidisciplinary panel comprised 58 neurocritical physicians and researchers with low attrition (12%). They were predominantly from Western regions (96%), actively involved in iMMM (82%), at least weekly (72.4%), with more than 10 years of specific experience (57%). Of the 127 items assessed for inclusion in COS and reporting guidelines, 45 (35.4%) reached strong and 8 (6.3%) moderate agreement. Main strong agreement items were: (i) demographics: age (98%) and sex/gender (90%); comorbidities: coagulation/platelet disorders (95%); initial scoring: Glasgow Coma Scale (97%) and pathology-specific scores (90%); active treatments: antithrombotics (95%) (ii) clinical practice: iMMM implantation indications (98%) and iMMM-guided interventions (91%); surgical practice: targeting strategies (97%) and concomitant external ventricular drainage (97%); technical details: recording modalities (98%); (iii) monitoring parameters: duration (97%) and triggered interventions (95%); standardized outcome reporting (93%); surgical complications (e.g., postoperative intracranial hemorrhages, CNS infections, and probe misplacement, all > 90%) and adverse events (accidental dislodgement, probe breakage, and technical malfunctions, all > 90%).

Conclusion This consensus establishes foundational COS and reporting guidelines for iMMM in neurocritical care. These harmonization tools can enhance research quality, comparability, and reproducibility, facilitating

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evidence-based practices for this emerging technology. However, challenges remain in developing purpose-specific guidelines and adapting them to diverse clinical and research settings.

Keywords Intracranial multimodal monitoring, iMMM, Multimodal neuromonitoring, MNM, Intracranial pressure, ICP, Brain tissue oxygenation, Pbto2, Microdialysis, Neurocritical care

Background

Neuromonitoring consists of an array of non-invasive and invasive modalities. Among these, intracranial multimodal monitoring (iMMM) involves the concurrent use of invasive techniques, such as intracranial pressure (ICP), brain tissue oxygenation ($PbtO_2$), cerebral blood flow (CBF), cerebral microdialysis, or intracranial electroencephalography (Table 1) to better investigate and characterize brain pathophysiology. Given its invasive nature and resource-intensive implementation, iMMM presents distinct technical, safety, and methodological challenges as cross-validation with non-invasive alternatives continues to evolve. However, despite its growing adoption in neurocritical care for clinical and research applications, the absence of standardization in indications, monitoring-guided protocols, and reporting has resulted in a heterogeneous body of literature, hindering collaborative efforts to establish evidence-based practices [1–3]. Core outcome sets (COS) and reporting guidelines are instrumental harmonization tools, offering structured frameworks for defining and reporting key outcomes, thereby enhancing research quality, comparability, and reproducibility [4, 5]. Here, we conducted an open, decentralized consensus study involving expert clinicians and researchers experienced in iMMM for neurocritical care to develop COS and reporting guidelines for future research.

Methods

A preliminary scoping literature review was conducted to map existing research, consensus, and guidelines related to iMMM in neurocritical care. Four co-investigators (S.B., M.A.B., N.T., and S.E.H.) searched PubMed, Embase, and Cochrane databases using the following keywords: ["intracranial multimodal monitoring" OR "invasive multimodal monitoring" OR "iMMM" OR "multimodal neuromonitoring" OR "MNM" OR "brain monitoring"] AND ["neurocritical care" OR "neurointensive care" OR "neuro ICU"].

A multidisciplinary, international consensus panel was established through the preliminary literature review for field contributors, communication channels within learned societies (i.e., Neurocritical Care and Neuro Anesthesiology French-Speaking Society; European Association of Neurosurgical Societies Trauma and Critical Care Section), and peer-to-peer recruitment. This panel was open to any qualified individuals with clinical or scientific expertise in iMMM for neurocritical care. Two co-investigators (M.A.B. and S.E.H.) confirmed this expertise, verifying each participant's credentials using open-source intelligence—i.e., publicly available institutional or biographic information and an author-based literature review while ensuring consistency with the participant's email address. In cases of discordance between co-investigators regarding expertise validation, additional documentation of clinical or research experience in iMMM will be requested from the potential participant.

Table 1 Common modalities of iMMM

Monitoring technique	Parameters measured	Key clinical applications	Common placement
Intracranial pressure (ICP)	Pressure (mmHg)	Management of intracranial hypertension, CPP targeting	Parenchymal, intraventricular
Brain tissue oxygenation ($PbtO_2$)	Oxygen partial pressure (mmHg)	Detection of brain tissue hypoxia, optimization of cerebral oxygenation	Parenchymal
Cerebral blood flow (CBF)	Regional blood flow (ml/100 g/min)	Assessment of cerebral perfusion, detection of ischemia	Parenchymal
Cerebral microdialysis (MD)	Metabolites concentrations (mmol/L)—e.g., Glucose, lactate, pyruvate, glutamate, glycerol	Metabolic monitoring, detection of energy crisis	Parenchymal
Intracranial electroencephalography(iEEG)	Electrical activity (µV, Hz)	Detection of cortical spreading depolarization, seizure monitoring	Parenchymal, cortical surface
Temperature	Local brain temperature (°C)	Fever detection, therapeutic hypothermia monitoring	Parenchymal

Between December 2023 and June 2024, we employed a three-round web-based modified Delphi technique to define a COS and reporting guidelines for iMMM in neurocritical care. Consent was implied by the experts' decision to complete the online surveys for the Delphi process. The study was deemed exempt from institutional review board approval. None of the experts had access to the participant list, preventing any consultation before responding. An initial questionnaire, formulated based on the preliminary literature review, consisted of multiple-choice and open-ended questions.

Each round of questions was distributed anonymously via email to ensure the experts were unaware of each other's identities and responses. Two investigators (M.A.B. and S.B.) supervised the process.

As a working basis, items were proposed in three domains: "patient characteristics" (demographics, comorbidities, initial scoring systems, and treatments), "practices" (clinical, surgical, and technical), and "outcomes" (iMMM use, surgical outcomes, complications, and adverse events). We defined iMMM for neurocritical care as the concurrent use of at least two invasive techniques to directly monitor intracranial parameters, assessing brain function and pathophysiology in critically ill patients. Herein, we refer to 'intracranial' as any monitoring occurring within the cranial cavity (including intraparenchymal, intraventricular, subdural, and intravascular spaces within cerebral vessels), and 'invasive' as any technique requiring surgical or endovascular breach of anatomical barriers (skin, skull, dura mater, or vessel walls) to access these spaces, thus including both direct transcranial and endovascular approaches while excluding external, surface or subcutaneous monitoring methods.

Each section included free-text fields to capture participant-driven insights or additional propositions, termed "add-ons," which were included in subsequent rounds. Add-ons were either directly incorporated into the next round, integrated with other propositions, or considered valuable insights without forming direct propositions based on a consensus among three investigators (S.B., M.A.B., and F.S.T.). Propositions endorsed by ≥ 75% of participants were classified as 'strong agreement' and included in the COS. Those with 50–75% endorsement were reconsidered in the subsequent round, requiring at least 66% for inclusion as 'moderate agreement.' Propositions with < 50% endorsement were considered lacking consensus and therefore excluded. Participants had the opportunity to request reconsideration of any included or excluded proposition. Each proposition was subject to a maximum of two consecutive rounds of consideration, either between rounds 1 and 2 or rounds 2 and 3. After each round, comprehensive group response feedback, along with the add-ons, were provided to the panel of participants in an "open report." To minimize response fatigue, each round's questionnaire was designed to be concise, taking less than 15 min to complete.

Results

The expert panel initially consisted of 58 neurocritical physicians and researchers, primarily from Europe (72%) and North America (24%); 57 of them participated in the second round, while the third round included 52 participants who provided full responses, for an overall dropout rate of 12%. Among first-round respondents, 47% were primarily clinicians (29% intensivists, 16% neurologists, 12% anesthesiologists); 40% neurosurgeons, and 3% were neuroradiologists. The majority of participants (83%) were actively involved in iMMM practice; 72% reported managing it on a daily or weekly basis, either in clinical (83%) and research (66%) roles. Over half of the participants (57%) had more than ten years of experience in iMMM. All participants' identities and expertise were unanimously validated by both co-investigators. Characteristics of the participants are outlined in Table 2.

Of the 127 items, 77 were initially provided, and 50 (39.4%) were derived from add-ons (Appendix 1). Agreement was reached on 54 items, with 46 achieving strong and 8 moderate levels.

Patient characteristics

Overall, 34 items (62%) did not reach agreement, three items (5%) achieved moderate agreement, and 18 items (33%) reached strong agreement (Table 3). Age (98%) and sex/gender (90%) were the most selected demographic variables in patient profiling. Comorbidities were considered important for reporting in research, with coagulation/platelet disorders (95%) and neurological conditions (88%) being the most frequently chosen. For initial scoring systems in assessing patient conditions, the Glasgow Coma Scale (GCS) (97%) and pathology-specific scores (90%), including the National Institutes of Health Stroke Scale (NIHSS) score (78%) and World Federation of Neurological Surgeons (WFNS) score (75%), were the most selected. Among active treatments, antithrombotics (95%) and anti-seizure medications (84%) were prioritized.

Practices for iMMM implementation

Overall, 20 items (53%) did not reach agreement, three items (8%) achieved moderate agreement, and 14 (37%) items reached strong agreement (Table 4). In clinical practice, the indication for iMMM implantation (98%) and iMMM-guided interventions (91%) were highly prioritized in patient care protocols. Similarly, established iMMM guidelines (87%) and data review protocols (87%)

Table 2 Characteristics of participants from the first round

Variables		Value n (%) N = 58
Main field of practice	Clinician	35 (60)
	Surgeon	23 (40)
Country of practice	Austria	3 (5)
	Belgium	4 (7)
	Canada	2 (3)
	Chile	1 (2)
	Finland	2 (3)
	France	11 (19)
	Germany	3 (5)
	Greece	1 (2)
	Italy	4 (7)
	Latvia	1 (2)
	Nepal	1 (2)
	Netherlands	1 (2)
	Serbia	1 (2)
	Spain	2 (3)
	Sweden	2 (3)
	Switzerland	6 (10)
	United Kingdom	1 (2)
	United States	12 (21)
Involvement in iMMM practice	Currently	48 (83)
	Previously	10 (17)
Type of involvement	Clinical	48 (83)
	Technical	14 (24)
	Research	38 (66)
Managing iMMM	Daily	24 (41)
	Weekly	18 (31)
	Monthly	5 (9)
	Yearly	1 (2)
Experience of iMMM practice (years)	< 5	11 (19)
	5–10	14 (24)
	10–15	14 (24)
	> 15	19 (33)

iMMM, intracranial multi-modal monitoring

were emphasized. In surgical practice, the iMMM targeting strategy for probe insertion (97%) and concomitant external ventricular drainage (EVD) (97%) received the highest agreement. Technical details related to iMMM, such as modalities recorded (98%) and time recording methods (86%), were also deemed crucial for reporting.

Reported outcomes

Overall, 16 items (52%) did not reach agreement, two items (6%) achieved moderate agreement, and 13 items (42%) reached strong agreement (Table 5). Duration of monitoring (97%) and interventions triggered by monitoring (95%) were identified as essential for reporting. Standardised reporting of clinical outcomes was strongly supported (93%), with agreement on the modified Rankin scale (mRS) (89%) and the Glasgow Outcome Scale-Extended (GOS-E) (83%) as preferred assessments. Complications, namely postoperative intracranial hemorrhages (98%), central nervous system (CNS) infections (97%), and misplacement of iMMM probes (95%), were strongly advocated for reporting. Any probe dislodgement (93%), breakage (91%), or malfunction (91%) was also deemed worthy of reporting.

Discussion

This open, decentralized, three-round multidisciplinary Delphi study involved 58 physicians and researchers. We established the Neurocore-iMMM framework, comprising COS (Appendix3) and reporting guidelines (Appendix 4) for iMMM in neurocritical care. Of 127 items, agreement was reached on 54, spanning the three domains of patient characteristics, clinical practices, and reported outcomes.

Beyond basic demographic variables, we identified critical baseline attributes for consistent patient profiling. Regarding comorbidities and treatments, strong agreement was reached on coagulation disorders, neurological conditions, cardiovascular diseases, organ failures, and diabetes, as well as the use of antithrombotics and antiseizure medications. These factors significantly affect intracranial physiology, ABI outcome, the risk profile for iMMM procedures, and the interpretation of neuromonitoring data, making their standardized reporting crucial [6–8].

The GCS achieved near-unanimous agreement with strong consensus on pathology-specific scores, particularly the NIHSS and WFNS, indicating the need for both general and tailored evaluation tools. Including premorbid mRS further emphasizes the importance of capturing pre-injury functional status. Interestingly, the imaging scores have yet to reach consensus, despite imaging's key role in assessing acute brain injuries. In addition, critical care scoring systems (e.g., APACHE, SAPS 2) and variables such as socioeconomic status, tobacco consumption, and BMI did not reach consensus—suggesting a preference for neurocritical care-specific measures and variables that directly impact acute clinical parameters in iMMM applications, as opposed to broad epidemiological characteristics.

Overall, our consensus on core demographic variables, key comorbidities, and validated baseline scoring systems underscores their importance in iMMM—a particularly resource-intensive and rapidly evolving multimodal form of invasive neuromonitoring. For instance, the Synapse-ICU study demonstrated the value of precise patient selection, focusing on severely brain-injured patients

Table 3 Patient characteristics

Question	Item	Selection rate (%)	Agreement
Which demographic data should be defined?	Age	98	strong
	Sex/gender	90	strong
	Drug use	48	no
	Hand dominance	48	no
	Alcohol consumption	46	no
	Race	46	no
	Body mass index	40	no
	Tobacco consumption	40	no
	Socioeconomic status	36	no
	Employment status	31	no
	Years of education	27	no
	Marital status	17	no
	Insurance coverage	5	no
Which comorbidities should be defined?	Coagulation/platelet disorders	95	strong
	Any neurological condition	88	strong
	Traumatic brain injury history	85	strong
	Cardiovascular diseases	83	strong
	Epilepsy history	83	strong
	Past neurosurgical procedures	80	strong
	Organ failure	79	strong
	Stroke history	78	strong
	Diabetes	76	strong
	Active infections	67	moderate
	Immunosuppression	62	no
	Active malignancies	59	no
Which initial scoring systems should be used?	Glasgow coma scale	97	strong
	Pathology-specific scores	90	strong
	Premorbid mRS	75	strong
	Injury severity score	60	no
	APACHE scores (II to IV)	45	no
	Frailty index	44	no
	Charlson comorbidity index	41	no
	SAPS 2 score	25	no
	ASA classification	22	no
	Karnofsky performance status	17	no
	Elixhauser comorbidity index	2	no

Table 3 (continued)

Question	Item	Selection rate (%)	Agreement
Which pathology-specific scores should be used?	NIHSS score	78	strong
	WFNS score	75	strong
	Modified fisher scale	72	moderate
	ICH score	56	no
	GCS-P score	48	no
	Hunt & Hess score	47	no
	Marshall score	42	no
	IMPACT score	42	no
	SOFA score	32	no
	Rotterdam score	29	no
	FOUR score	23	no
	Markwalder scale	14	no
	rCAST score	8	no
	BNI score	6	no
Which active treatments should be defined?	Antithrombotics	95	strong
	Anti-seizure	84	strong
	Corticosteroids	73	moderate
	Antibiotics	64	no
	Implantable devices	43	no

APACHE, acute physiology and chronic health evaluation; ASA, American Society of Anesthesiologists; BNI, Barrow Neurological Institute; FOUR, full outline of UnResponsiveness; GCS-P, glasgow coma scale pupil score; ICH, intracerebral hemorrhage; iMMM, intracranial multi-modal monitoring; mRS, modified rankin score; NIHSS, National Institutes of Health Stroke Scale; rCAST, revised post-cardiac arrest syndrome for therapeutic hypothermia; SAPS, simplified acute physiology score; SOFA, sequential organ failure assessment

with few comorbidities deemed potentially salvageable based on clinical assessments and scoring systems [9]. However, variability in agreement on baseline characteristics reflects ongoing differences in clinical practice and research priorities. Standardizing the assessment of brain injury severity, pre-morbid conditions, and functional status is crucial to enhancing comparability across studies, addressing confounding factors in outcome assessments, and prognostic studies to improve patient selection [10, 11].

A strong consensus emerged on defining core elements of iMMM use, including its indications, guideline-based interventions, and data review protocols, emphasizing the need for standardization to develop evidence-based criteria [3]. Main priorities include distinguishing observational from interventional approaches, defining iMMM-derived secondary brain injury, and establishing protocols for imaging, recording, and infection documentation. Similarly, arterial line leveling reached strong agreement, highlighting its central role in CPP interpretation and the need for its standardized reporting [12]. Leveling at heart (phlebostatic axis) versus the ear (tragus) can result in a 10–15 mmHg difference in mean arterial pressure, complicating CPP threshold determination when aggregating trial data without accounting for leveling site [13]. No international consensus exists on this issue, apart from French 2018 recommendations and a 2014 British joint statement to use the ear tragus level [14, 15]. Notably, some critical clinical practices only reached moderate agreement, such as preoperative medication reversal, while the initiation of antiseizure therapy did not achieve consensus. This variation may reflect differences in clinical contexts, institutional protocols, and research priorities in iMMM implementation, highlighting the need for dedicated investigations to gather detailed insights and inform the development of specific guidelines [16].

In surgical practices, there was strong consensus on iMMM insertion targeting strategies, concomitant EVD, and operative settings. Properly defining these critical factors will help delineate iMMM accuracy and safety better, ensuring consistency in the reliability, collection, and interpretation of the neuromonitoring data. While probe surgical fixation methods reached a moderate agreement, implantation depth and other significant surgical details did not achieve consensus.

Table 4 Practices for iMMM implementation

Question	Item	Selection rate (%)	Agreement
In clinical practice, what should be defined?	iMMM implantation indication	98	strong
	iMMM-guided interventions	91	strong
	Use of established iMMM guidelines	87	strong
	Data review protocol	87	strong
	Monitoring approach: Observational vs. interventional	86	strong
	iMMM-derived definition of secondary brain injury	79	strong
	iMMM-related imaging protocol	78	strong
	Use of iMMM recording protocol	78	strong
	Protocol for documenting a suspected iMMM-related infection	76	strong
	Arterial line levelling site	76	strong
	Preoperative medication reversal	69	moderate
	Preoperative prophylactic drug treatment	62	no
	Initiation of anti-seizure therapy	60	no
	Preoperative invasive monitoring (extra-cranial)	45	no
	Local caseload of iMMM practice	42	no
	Preoperative sedative agents	41	no
	Dressing of the iMMM	33	no
In surgical practice, what should be defined?	Targeting strategy	97	strong
	Concomitant EVD implantation	97	strong
	Implantation settings (OR vs. bedside)	88	strong
	Probes surgical fixation method	66	moderate
	Implantation depth of the probes	64	no
	Craniotomy dimension	46	no
	Number of burr-holes	46	no
	Closure technique	42	no
	Cranial drill used for the burr-hole	31	no
	Durotomy technique	31	no
	Navigation devices for implantation	0	no
Which technical details should be defined?	Modalities recorded	98	strong
	iMMM time recording (i.e., continuous or intermittent) for each modality	86	strong
	iMMM (re)calibration protocol	73	moderate
	Technical specificities of the probes	59	no
	Technical specificities of the iMMM data recording systems	55	no
	iMMM bedside presentation for neurocritical caregivers	55	no
	Manufacturer's material specifications	55	no
	Technical specificities of the iMMM fixation device	48	no
	Device regulatory details (e.g., CE/FDA-approval)	43	no
	Probe(s) fixation method	2	no

EVD, external ventricular drain; OR, operating room

Lack of consensus, similar to the variation observed in clinical practice, may be attributed to differing surgical techniques and their perceived importance—further compounded by the minority representation of surgeons in our panel. These findings underscore the need for specific surgical guidelines to improve iMMM implantation techniques and related research.

From a technical perspective, strong consensus was reached on reporting recorded modalities and time recording methods, while (re)calibration protocols achieved moderate agreement, thus emphasizing the fundamental importance of these elements for data integrity and comparability. Several technical details failed to reach a consensus, including probe and recording system

Table 5 Reported outcomes for iMMM

Question	Item	Selection rate (%)	Agreement
What should be defined during the monitoring	Duration of monitoring	97	strong
	Triggered interventions	95	strong
	Indication of early withdrawal of iMMM	84	strong
	Withdrawing/withholding of critical care and life-sustaining therapies	81	strong
	Time-specific monitoring patterns related to presumed pathophysiological changes	66	moderate
	Cumulative intervals of abnormal recording/technical failure	62	no
Which surgical outcomes should be defined?	Probe repeated insertion	74	moderate
	iMMM placement taking place in primary or secondary neurosurgery	63	no
	Operative timing (door-to-surgery)	55	no
	Surgery duration	48	no
	Surgeon's expertise	38	no
Should outcomes be reported in a standardised way?	Yes	93	strong
	No	4	no
	No opinion	3	no
If so, which indicators should be used?	mRS	89	strong
	GOS-E	83	strong
	Pediatric GOS-E revision	35	no
	CRSR-FAST	26	no
	GOS	20	no
	FSE	20	no
	PCPC	17	no
Which complications of iMMM should be reported?	All	49	no
	Significant ones (i.e., impacting on care)	49	no
	No opinion	2	
If reporting surgical complications of iMMM, which ones should be considered?	Postoperative intracranial hemorrhages	98	strong
	Infection of CNS	97	strong
	Probe(s) misplacement	95	strong
	Intracranial bone fragments	60	no
	Pneumocephalus	48	no
Which adverse events of iMMM should be defined?	Accidental dislodgement	93	strong
	Breaking of probes and/or fixation method	91	strong
	Technical/hardware malfunction	91	strong

CNS, central nervous system. CRSR-FAST, coma recovery scale-revised for accelerated standardized assessment. FSE, functional status examination. GOS-E, glasgow outcome scale-extended. iMMM, intracranial multi-modal monitoring. mRS, modified Rankin scale. PCPC, pediatric cerebral performance category

specificities, manufacturer specifications, and regulatory information. The absence of consensus may stem from the lesser perceived importance of these technical aspects for clinical or research purposes, combined with the underrepresentation of technical experts, such as engineers, basic neuroscientists, and neurophysiologists, on our panel. Dedicated efforts to establish technical consensus could be essential to ensure technological reliability and effective implementation. Additionally, standardized validation and surveillance of iMMM devices throughout their development and clinical application may benefit from the involvement of regulatory compliance experts.

Our consensus strongly supported using standardized outcomes in iMMM research, with most experts agreeing on using established scales. The mRS and GOS-E were preferred assessments. This aligns with the overarching aim in neurocritical care to standardize outcome measures, enabling cross-study comparisons and meta-analyses and enhancing the quality of evidence while accounting for patient heterogeneity and disease severity in iMMM [17, 18].

Defining the duration of monitoring and interventions triggered by iMMM was prioritized, emphasizing their importance in understanding the temporal dynamics of patient management and how iMMM influences clinical decision-making. These data are essential, as monitoring parameters provide high-resolution physiological information, enabling patient-tailored interventions [19]. There was also strong consensus on documenting early withdrawal of iMMM and decisions to withdraw or withhold critical care and life-sustaining therapies. Indeed, defining and reporting these decisions are crucial to mitigate selection and confirmation biases that can affect outcome assessments in severe brain injury cases, where care limitations based on perceived poor prognosis may lead to self-fulfilling prophecies [20–24]. Improving our understanding of these drivers is also important for future clinical trial design.

Complications, including postoperative intracranial hemorrhages, CNS infections, and probe misplacement, were identified as critical to define. Adverse events, such as accidental probe dislodgement, probe breakage, and technical malfunctions, were also underscored, further highlighting the importance of monitoring system reliability and robustness to ensure data integrity. However, the perfect split on whether to report all complications or only those significantly impacting care exemplifies the challenge of balancing comprehensive research standardization with practical applicability. Without evidence-based data, one can not fully define the clinical significance of certain complications beforehand. Thus, extensive studies investigating varied complications, supported by standardization efforts, will be essential to delineate iMMM's safety profile and inform risk–benefit assessments in clinical practice and future trial design. Indeed, iMMM—an invasive procedure in frail, injured brains—carries significant risks of complications that may affect expected outcomes. In the OXY-TC trial, six patients (4%) in the iMMM group experienced intracerebral hematomas due to probe placement, potentially altering trial results [25].

Several proposed outcome measures, such as cumulative intervals of abnormal recordings and various surgical outcomes, did not achieve consensus—likely influenced by the minority participation of surgeons and technical experts in our panel, as previously discussed. Standardized outcomes are critical for improving consistency across institutions and promoting the adoption of validated measures in clinical practice, thereby supporting robust long-term studies on iMMM's impact [26, 27].

Our consensus aligns with broader efforts, including the NIH/NINDS Common Data Elements project, which are focused on enhancing research quality, reproducibility, and interoperability [3, 28–37]. This study establishes a foundational consensus on iMMM, providing both a stepping stone and a broad framework to develop specific standards guiding iMMM development, application, and validation for evidence-based practices. Distinctively, we adopted an open, decentralized framework tailored to iMMM, addressing its specific needs and challenges in research standardization. Of course, several significant challenges persist in achieving this objective.

The rationale of iMMM is to identify and characterize actionable endotypes of secondary brain injury, enabling targeted interventions. With this aim, dedicated standards could promote phenotype-specific treatments [38]. However, defining and measuring secondary brain injuries remains challenging due to the complexity of brain pathophysiology and the transdisciplinary integration required to validate biomarkers. In fact, iMMM relies on regional probes sampling small brain tissue volumes, making precise targeting strategies crucial for consistent data acquisition, reporting, and interpretation. Nevertheless, no consensus exists on optimal probe placement, even for $PbtO_2$, the most widely used modality besides ICP [39, 40]. Studies vary in targeting strategies—such as selecting the nondominant hemisphere, normal-appearing parenchyma, or perilesional at-risk tissue—yet many fail to specify these strategies, and the probe's location and the injury's nature can significantly influence data interpretation and clinical management [40]. Beyond placement, this heterogeneity also extends to iMMM thresholds for initiating therapeutic interventions, requiring standardized definitions. This is compounded by the difficulty of integrating multiple regional iMMM data streams with global monitoring modalities, where conflicting physiological states may coexist [41]. To date, evidence is quite limited, with most studies focusing on single monitoring modalities—a recent review identified 43 studies using more than one modality in TBI patients, and only three specifically examined the impact of iMMM on clinical management [2]. Notably, a single-center quasi-experimental study of 113 severe TBI patients demonstrated that combining iMMM with neurointensivist consultation improved 6-month functional outcomes, providing a model for evaluating the clinical utility of iMMM-guided management [42]. With the recent release of the OXY-TC trial and the ongoing BOOST3 and BONANZA phase 3 trials, high-level evidence may soon strengthen our practices [25, 43, 44].

An epitome of these challenges is the pediatric application of iMMM [45]. TBI, as an example, is a leading cause of morbidity and mortality in children, but determining appropriate monitoring thresholds is challenging due to dynamic changes in cerebral physiology, such as variations in CBF and brain compliance during development [46]. Brain compliance is higher in infants

with patent fontanelles, while CBF rises in early childhood before declining in adolescence. Although current guidelines provide general thresholds, they are based on class III evidence and may not be optimal across all ages, highlighting the potential of iMMM for personalized interventions [47, 48]. However, surgical implantation of iMMM in children is complicated by anatomical factors such as skull thickness, and the safety of multilumen bolts remains uncertain [1]. Along these lines, validating non-invasive neuromonitoring modalities against iMMM could particularly benefit this population. Notably, most experts in our panel were adult practitioners, likely contributing to the limited selection of pediatric outcome measures. This underscores the challenge of creating guidelines that are both broadly applicable and precise enough for specific real-world needs, requiring targeted research and consensus for diverse populations, including children.

In parallel, the rapidly advancing technological landscape, driven by breakthroughs in brain-machine interfaces, bioelectronics, and material science, presents both opportunities and challenges for neurocritical care [49–51]. Innovations in probe design, signal processing, and machine intelligence offer the potential for more precise, real-time monitoring of brain physiology [52–58]. However, our community must be prepared for this technology transfer by being able to critically evaluate and effectively integrate these neurotechnologies [59].

In conclusion, the limited and heterogeneous state of current iMMM research, combined with the emerging, resource-intensive nature of its technology, emphasizes the critical need for structured collaborative efforts to drive progress in this field. To address these challenges, we propose the three following future directions for dedicated working groups:

- Expanding the effort to devise pathology-specific (e.g., TBI, SAH), population-based (e.g., adults, children), purpose or setting-dependent (e.g., observational vs interventional, resource-constrained), and discipline-focused (e.g., neurophysiology, neurosurgery) guidelines with practice-specific procedures for data collection, review, interpretation, and intervention guidance.
- Tracking progress in neurotechnologies relevant to iMMM, focusing on non- and minimally invasive modalities.
- Modeling iMMM-specific computational frameworks based on regional and global parameters, integrating spatial and endotype heterogeneity across the spectrum of acute brain injuries.

An open, decentralized approach is essential to advance iMMM development, fostering accessibility, inclusivity, and broader transdisciplinary collaboration. Establishing a dedicated platform for open collaboration would facilitate cooperation among researchers, clinicians, technology developers, and various stakeholders, supporting continuous consensus-building and providing vital research tools—such as prospective registries, shared databases, and comprehensive documentation—for external validation and updates of the Neurocore-iMMM guidelines. This model has been successful in other fields, particularly basic neuroscience, ensuring that frameworks remain current with technological advancements to accelerate the translation of emerging neurotechnologies into clinical practice [60–62]. It may also address the slower progress of iMMM—one of the earliest clinical-grade brain-machine interfaces—as compared to other precision neurotechnologies, which in part may be related to lower commercial incentives.

Limitations

Despite active outreach efforts to Asian, Australian, and African colleagues through our open, decentralized approach, participation remained largely Western, reflecting both the resource-intensive nature of iMMM and inherent network preferential attachment in academic collaboration. Indeed, the expert panel, predominantly composed of clinicians from Europe and North America who mostly practice in academic centers, may introduce geographic and institutional bias, limiting the global applicability of our findings. In addition, the underrepresentation of surgical, pediatric, and technical specialties with the non-inclusion of nurses may have further constrained perspectives and generalizability across all levels of healthcare delivery. Along these lines, the absence of patients and their representatives precluded the integration of patient-reported outcomes and experiences. While effective, consensus-building through the Delphi technique has intrinsic limitations [63, 64]. Lastly, although expert consensus is valuable, it is based on opinion and should not be conflated with empirical data.

Conclusions

The Neurocore-iMMM framework lays a foundation for harmonizing iMMM in neurocritical care and research by establishing COS and reporting guidelines. However, significant challenges persist, particularly in developing pathology-specific guidelines and adapting to various populations, purposes, and settings. The proposed open, decentralized platform for ongoing collaboration seeks to refine these guidelines continuously, ensuring they evolve with advances in neurotechnology while meeting

diverse needs. Future efforts should focus on empirically validating these recommendations to confirm their global utility.

Abbreviations

APACHE	Acute physiology and chronic health evaluation
ASA	American Society of Anesthesiologists
BNI	Barrow Neurological Institute
CBF	Cerebral blood flow
CE	Conformité Européenne
CNS	Central nervous system
COS	Core outcome sets
CRSR-FAST	Coma recovery scale-revised for accelerated standardized assessment
EVD	External ventricular drain
FDA	Food and drug administration
FSE	Functional status examination
GCS	Glasgow coma scale
GCS-P	Glasgow coma scale pupil score
GOS-E	Glasgow outcome scale—extended
ICH	Intracerebral hemorrhage
ICU	Intensive care unit
iMMM	Intracranial multimodal monitoring
NIHSS	National Institutes of Health Stroke Scale
OR	Operating room
PCPC	Pediatric cerebral performance category
$PbtO_2$	Brain tissue oxygenation
rCAST	Revised post-cardiac arrest syndrome for therapeutic hypothermia
SAPS	Simplified acute physiology score
SOFA	Sequential organ failure assessment
TBI	Traumatic brain injury
WFNS	World Federation of Neurological Surgeons

Supplementary Information

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Supplymentary Material 1.

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Author contributions

SB, MAB, and FST are chief investigators. SB, MAB, SEH, CR, FST, VR, BA, FB, RC, FAM, MK and DP drafted the manuscript. SB, MAB, FT and NM conceived the study concept and design. All authors of the Neurocore-iMMM Research Group collected the data by participating in the three rounds. All authors of the Neurocore-iMMM Research Group had access to the study data through publicly available open reports. SB, MAB, FST, CR, NM, AG, FB, BA, and MP contributed to the analysis and interpretation of the data. SB, MAB, FST, CR, FB, CL, FB, GC, NT, CR, NBH, LN, TVH, SP, SH, MM, MK, EG, VR, FAM, BF, PH, EA, AN, AG, BA and RH contributed in reviewing and editing of the final manuscript. All authors reviewed and approved the final manuscript. SB and MAB contributed equally.

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Availability of data and materials

The Neurocore-iMMM study data are available upon request. Requests for data can be made at any time and can be initiated by contacting samibarrit@gmail.com.

Declarations

Ethical approval and consent to participate

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Consent for publication

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